REMARKS

Claims 1-7 are pending. Claims 3 and 4 have been withdrawn from consideration.

In the Office Action mailed February 18, 2009, claims 1, 2 and 5-7 have been rejected as allegedly obvious under 35 U.S.C. § 103 over U.S. Patent No. 6,150,500 to Salerno ("*Salerno*") in view of *Davenas* et al., *Epshtein* et al., and *Feldman* et al. (of record). Newly presented Claims 6-7 were joined to the rejection of record. Claims 1, 2 and 5 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by *Davenas* et al. and *Epshtein* et al. Claims 1, 2 and 5-7 were rejected under 35 U.S.C. § 112 as indefinite.

By this Amendment, Applicants amended claims 1, 2, 5-7 and added new claims 8-10. Support for new claims 8-10 may be found in the specification and claims as filed. No new matter has been added. Applicants respectfully request reconsideration and allowance of all pending claims in view of the amendments and remarks set forth below.

I. AMENDED CLAIM 1 IS SUPPORTED IN THE APPLICATION AS FILED

As amended, claim 1 now recites:

> 1. (Currently Amended) A medicament for treating erectile dysfunction comprising a homeopathically potentised form of monoclonal, polyclonal, or natural antibody to an endothelial nitric oxide synthase (NO synthase).

Applicants are fully aware that the newly added limitation "homeopathically potentised" is not set forth in the application in *ipsis verbis*. For this reason and to advance the prosecution on the merits, Applicants wish to address the issue preemptively and directly for Examiner's consideration.

Applicants note that *haec verbis* disclosure is not a pre-requisite for complying with the written description requirement. *See* MPEP § 2163. I. B. The description may be express, implicit, or inherent. *Id.* The key to evaluating compliance with the written description requirement is a determination whether the applicant had possession of the claimed invention based on the content of the application as a whole. *See* MPEP § 2163. II. The outcome of the

evaluation depends on whether "the description clearly allows persons of ordinary skill in the art to recognize that he or she invented what is claimed." *See* MPEP § 2163.01, *citing In re Gostelli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989).

The specification describes: a) preparation of "potentiated" or "activated" antibodies to NO synthase by homeopathic technology (*e.g.*, page 2, paragraphs 5-6), b) administration of the activated or potentiated form of the NO synthase antibody to patients (*e.g.*, Example 3), and c) biological effects of such administration (*e.g.*, Example 3). In combination, these disclosures clearly place "homeopathically activated form" of the antibodies in possession of the inventors as of the filing date of the above-identified application.

Therefore, Applicants respectfully submit that amended claims 1, 2 and 5-7 and new claims 8-10 are fully supported in the application as filed.

II. OBVIOUSNESS REJECTION OVER *SALERNO* IN VIEW OF *DAVENAS ET AL., EPSHTEIN,* ET AL. AND *FELDMAN ET AL.*

The Examiner has rejected claims 1, 2 and 5-7 as allegedly obvious over *Salerno* in view of *Davenas* et al., *Epshtein,* et al. and *Feldman* et al. In the Office Action, the Examiner appears to suggest that one skilled in the art would be motivated to combine *Salerno* with *Davenas* et al. and/or *Epshtein* et al. based on the motivation of *Feldman*, et al. - *i.e.*, use the antibodies to NO synthase as disclosed by *Salerno* in the manner disclosed in *Epshtein* et al. and/or *Davenas* et al. to arrive at the medicament of the present invention. The Examiner also suggests that one skilled in the art would have a reasonable expectation that such combination/modification would be successful.

Applicants strongly and respectfully disagree. As amended claims 1, 2 and 5-7 and new claims 8-10 are directed to homeopathically potentised form of antibodies to an endothelial nitric oxide synthase (NO synthase).

Salermo discloses antibodies to NO synthase at normal concentration. Davenas et al. teach

that degranulation of basophils contained in leukocyte suspensions was induced by diluted anti-IgE antibody. *Feldman* et al. disclose the treatment of rheumatoid arthritis with anti-TNF antibodies in conjunction with anti-CD4 antibody and disclose that a benefit of combination treatment is that lower dosages can be used which outcome is economically advantageous. *Epshtein* et al. disclose an effect of ultra-low doses of antibodies to brain-specific antigen (S-100) on behavior characteristics in rat. *Epshtein* et al. report that administration of the antibody led to changes in rat behavior for a partial group of rats in the study (for example, an increase in the latent period of the emotional reflex reaction).

To set forth a *prima facie* case of obviousness, the Examiner must show that one skilled in the art would have a reasonable expectation that the combination of *Salerno* and *Epshtein/Davenas* will be successful. *See* § MPEP 2143.02. Meeting the burden requires that the prior art provides some degree of predictability. *Id., citing In re Rhinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). In the pharmaceutical arts, the expectation of success is reasonable when the prior art as a whole would lead one skilled in the art to believe that the claimed invention would at least have activity of some type for the stated purpose. *In re O'Farrell*, 853 F.2d 984, 903 (Fed. Cir. 1988), *In re Merck*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). The Court of Appeals for the Federal Circuit suggested that finding of reasonable expectation of success for a pharmaceutical product requires an expectation of activity greater than a baseline level of activity. *Yamanouchi Pharmaceutical, Inc. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1345 (Fed. Cir. 2000).

Applicants respectfully submit that none of the references, alone or in combination, disclose, teach or suggest anything that would lead one skilled in the art to expect that a homeopathically activated form of an antibody to NO synthase would have any activity, let alone the specific activity levels observed. *Epshtein* et al. does disclose that an activated form of an antibody to brain-specific antigen has some effect on rat behavior. How does this lead one skilled in the art to expect any activity of homeopathically activated antibodies to NO synthase, let alone the specific activity observed? None of the references, including Salerno, *Epshtein* et al. or *Davenas* et al., disclose a mechanism of action for the potentiated antibodies, *or contain any other information that would suggest to an artisan that what works for one type of antibodies would work for another.* While Applicants are well aware of the decision of the United States Supreme

Court in *KSR Int'l v. Teleflex, Inc.* 127 S. Ct. 1727 (2007), the facts of the present case have nothing to do with a situation where "there are a finite number of identified, predictable solutions," when "a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp." *KSR Int'l* at 1742. As it is well-known to those skilled in the art, the universe of various antigen-antibody pairs is nearly limitless.

Furthermore, to set forth a *prima facie* case of obviousness, the Examiner must show that the prior art taken in its entirety provides a reason for one skilled in the art to arrive at the invention as a whole. MPEP § 2141.02. It is improper to focus on the specific difference between the prior art and the invention as such. *Id.* The question is whether the prior art in its entirety provides "an apparent reason to combine the known elements in the fashion claimed by the patent at issue." *KSR Int'l* at 1742. Considering the invention as a whole, the entirety of the prior art did not provide such "apparent reason." The Examiner pointed to *Feldman*'s teaching that lower doses of antibodies would "offer the advantage of lower financial costs to the patient," and asserted that this *Feldman* statement would provide a motivation to one skilled in the art to move in the direction of the claimed invention. As the specification of the present application makes explicitly clear, the claimed medicament contains "homeopathically activated form" of an antibody. The difference between the "homeopathically activated form" and the form of *Feldman* is not simply quantitative (as the Examiner appears to suggest). The difference is qualitative. At most, *Feldman* suggests a reduction in the traditional dose is a benefit of combination therapy. How such reduction provides "an apparent reason" to cross the barrier from traditional doses to the qualitatively and intrinsically different form claimed in the amended claim 1?

Applicants submit hereby a Declaration by Dr. Oleg Epshtein ("the *Epshtein Declaration I*"). The *Epshtein Declaration I* is submitted as evidence in further response to Examiner's allegations of *prima facie* obviousness. The *Epshtein Declaration I* is submitted to show absence of *prima facie* obviousness, not in rebuttal of the alleged *prima facie* case. In the *Epshtein Declaration I*, Dr. Epshtein states that one skilled in the art would not expect that a homeopathically activated form of an antibodies to NO synthase would be active for intended purpose based on the information provided in the prior art at the time the '650 application was filed. Applicants respectfully assert that the *Epshtein Declaration I* is un-rebutted evidence of

non-obviousness, and it provides further support for non-obviousness of amended claims 1, 2, 5-7 and new claims 8-10.

Applicants respectfully suggest the Examiner did not put forth a *prima facie* case of obviousness with respect to claims 1 and 6, as amended and dependent claims.

While Applicants believe that the evidence in the file wrapper does not support *prima facie* obviousness of amended claims 1, 2, 5-7, Applicants wish to submit rebuttal evidence to advance the prosecution on the merits. Attached herewith is another Declaration by Dr. Epshtein ("the *Epshtein Declaration II*") that includes evidence that the claimed invention yields unexpected properties and that the medicament of the present invention based on homeopathic dilution of antibodies to NO synthase is statistically far more effective than placebo (water). Furthermore, while not necessary to establish patentability, the study also demonstrated that the homeopathically activated form of antibodies to NO synthase is at least as effective as or more effective than sildenafil, a well-known and accepted pharmaceutical compound used in treating erectile disfunction. For example, the difference in intromission rate between subjects treated with the homeopathic dilution of antibodies to NO synthase, sildenafil and the control subjects is undoubtedly statistically significant ($p<0.05$) and cannot be ascribed to anything other than the unexpected and superior activity of the claimed preparation. Applicants respectfully assert that the *Epshtein Declaration II* is un-rebutted evidence of non-obviousness, and it provides further support for non-obviousness of claims 1, 2 and 5-7. Would one skilled in the art expect the magnitude and nature of effect described? Epshtein Declarations I & II which are the evidence now in the file, clearly established that the answer is in the negative.

Applicants respectfully submit that none of the references, alone or in combination, disclose, teach or suggest anything that would lead one skilled in the art to expect that a homeopathically activated form of an antibody to NO synthase would have any activity, let alone the specific activity levels reported in the *Epshtein Declaration II*.

On the basis of the foregoing, Applicants respectfully submit that claims 1 and 6, as amended and dependent claims are non-obvious. Withdrawal of the rejection is respectfully requested.

III. REJECTION OF NEWLY PRESENTED CLAIMS 6 AND 7

Claims 6 and 7 were joined to the rejection of record in that claim 6 recites that the antibody corresponds to a fragment, which language is interpreted to be an open sequence language. The Examiner also indicated that claim 6 contains the indefinite article "a" rather than the definite article "the" in reference to the peptide sequence.

Claim 6 has been amended to eliminate the indefinite article "a" and to identify the exact sequence of the fragment. Thus, Claim 6 as amended recites a medicament for treating erectile dysfunction comprising homeopathically potentised form of monoclonal, polyclonal, or natural antibody to a fragment of nitric oxide synthase (NO synthase), having SEQ ID NO:1.

Applicants respectfully submit that claim 6 as amended and dependent claim 7 are non-obvious. Withdrawal of the rejection is respectfully requested.

IV. ANTICIPATION REJECTIONS OVER DAVENAS ET AL. AND EPSHTEIN ET AL.

The Examiner has rejected claims 1, 2 and 5 as allegedly anticipated by Davenas et al. and Epshtein et al. As amended claim 1 recites:

> 1. A medicament for treating erectile dysfunction comprising a homeopathically potentised form of monoclonal, polyclonal, or natural antibody to an endothelial nitric oxide synthase (NO synthase).

To anticipate a claim, a reference must disclose, either explicitly or inherently, each element of the claim. *Verdegaal Bros. v. Union Oil Co. of Cal.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The prior art cited by the Examiner does not disclose each and every element of rejected claim 1, either explicitly or inherently.

Nothing in *Davenas et al.* teaches anything related to homeopathy, let alone to "homeopathically activated form of antibodies to NOS." Withdrawal of the anticipation rejection is respectfully requested.

Epshtein et al. discloses an effect of ultra-low doses of antibodies to brain-specific antigen (S-100) on behavior characteristics in rat. *Epshtein et al.* does not teach anything homeopathically activated form of antibodies to NOS. Withdrawal of the anticipation rejection is respectfully requested.

V. INDEFINITENESS REJECTION OF CLAIMS 1, 2 AND 5-7

The Examiner rejected claims 1, 2 and 5-7 as indefinite in that the claims recite "potentiated antibodies to NO synthase" and then proceed to recite that the potentiated antibodies do not bind NO synthase. The Examiner further states that there are numerous NO synthases and reciting a fragment by its position within a larger amino acid sequence without identifying the exact sequence renders the claim uncertain.

As amended claim 1 does not recite that the antibodies do not bind NO synthase. Claims 6 has been amended to recite antibody to a fragment of nitric oxide synthase (NO synthase), having SEQ ID NO:1. As such, it is clear that the exact sequence of the fragment is clearly identified.

In view of the foregoing, the Applicants submit that all claims are in condition for allowance. Accordingly, both reconsideration of this application and its swift passage to issuance are earnestly solicited. In the event that there are any fees due and owing in connection with this matter, please charge the same to our Deposit Account No.50-4711

Respectfully submitted,

Dated: August 13, 2009

By:/Edward D. Pergmanet/
Edward D. Pergament
(Reg. No. 43,346)
Attorney for Applicant(s)

K:\Clients\Epshtein, Oleg Dr. -841\841-006\841-006_Amendment.doc